



Trichloroethylene

White Paper

Executive Summary

Trichloroethylene is believed to have been discovered in 1864 and was first commercially produced in Germany in the early 1900s. It has been commonly used for cleaning of metals and other parts since the introduction of the vapor degreasing process in the early 1930s and continues to be the standard by which other cleaning processes are compared. Today, its primary uses are as an intermediate in the production of hydrofluorocarbon refrigerants and as a cleaning agent.

The health effects of trichloroethylene have been studied extensively. The most significant findings to come out of the many long-term animal studies of the chemical are that it has caused liver and lung tumors in mice. The significance of these tumors to human health is unclear due to species differences in both trichloroethylene metabolism and reaction to the metabolites. This is supported by epidemiology studies of workers exposed to trichloroethylene that generally indicate no overall increase in cancer risk. Although recent studies of a small population of exposed workers in Germany appear to show an increase in kidney cancer, these studies suffer from major design flaws and are inconsistent with the results of larger, better conducted studies.

The International Agency for Research on Cancer (IARC) currently considers trichloroethylene to be "probably carcinogenic to humans" (Group 2A), based on its conclusions that there is "limited" evidence of carcinogenicity in humans. The epidemiological data base for trichloroethylene is considered by the American Conference of Governmental Industrial Hygienists (ACGIH), however, to support classification in Group A5 (Not Suspected as a Human Carcinogen) "since the substance has been demonstrated by well controlled epidemiological studies not to be associated with any increased risk of cancer in exposed humans." The U.S. Environmental Protection Agency currently is conducting a reassessment of the carcinogenic potential of trichloroethylene.

Introduction

Trichloroethylene is used widely by industry as a metal degreaser. It is especially valuable because of its cleaning properties, low flammability, and lack of a measurable flashpoint. Trichloro-

ethylene also is used as a chemical process intermediate in fluorochemical and polyvinyl chloride (PVC) production. It has been used worldwide for more than 70 years.

Trichloroethylene, a colorless, volatile liquid, is an unsaturated aliphatic halogenated hydrocarbon. In the United States, it is produced by The Dow Chemical Company and PPG Industries, Inc. In 1998, U.S. demand was about 171 million pounds (77,700 metric tons) of which about 15 million pounds (6,800 metric tons) were imported. About 84 million pounds (38,000 metric tons) were exported.

Uses

Use of trichloroethylene by U.S. industry in 1999 can be broken down in the following manner:

chemical intermediate	54%
metal cleaning/degreasing	42%
miscellaneous	4%

Chemical Intermediate

High-purity grades of trichloroethylene are used as a feedstock in the synthesis of the refrigerant hydrofluorocarbon 134a. In this process, the trichloroethylene molecule is destroyed to form the new fluorinated compound. It also is used in the production of such chlorinated end products as polychlorinated aliphatics and flame-retardant chemicals. In polyvinyl chloride (PVC) manufacture, trichloroethylene is used as a molecular-weight control agent.

Metal Cleaning and Degreasing

Among the properties that have contributed to trichloroethylene's wide acceptance as a metal cleaner and degreaser are the following:

- high solvency
- low flammability
- non-corrosiveness
- high stability
- low specific heat
- low boiling point
- low latent heat of vaporization

Trichloroethylene's advantages for metal cleaning include the ability to degrease more thoroughly and several times faster than alkaline cleaners, and its compatibility with smaller equipment that consumes less energy. Trichloroethylene is an important solvent for degreasing aluminum and for cleaning sheet and strip steel prior to galvanizing. Trichloroethylene also is used for cleaning liquid oxygen and hydrogen tanks.

Commercial trichloroethylene formulations include a stabilizer system to help prevent solvent breakdown caused by contaminants such as acids, metal chips and fines, and exposure to oxygen, light, and heat.

Miscellaneous

Trichloroethylene is used as a solvent in some nonflammable adhesive and aerosol formulations, and as a low temperature heat-transfer medium. Other applications of trichloroethylene include its use as a solvent in the metal processing, electronics, printing, pulp and paper, and textile industries.

Health Effects

General

Acute (short-term) overexposure to trichloroethylene vapor can cause central nervous system effects (e.g., light-headedness, drowsiness, headache, giddiness) which may lead to unconsciousness or prove fatal in extreme circumstances. Also, at very high exposure levels, trichloroethylene can sensitize the heart to the effects of adrenaline and similar agents, which may lead to sudden cardiac arrest. In addition, trichloroethylene may irritate the respiratory tract at high vapor concentrations. Repeated or lengthy contact with the chemical in liquid form can cause irritation of the skin and eyes.

Chronic (repeated) overexposure, well in excess of recommended occupational limits, has been associated with damage to the liver and kidneys, although this is less well documented in humans than in animals.

Genotoxicity

Trichloroethylene has been tested for its mutagenicity (genotoxicity) in a number of assays in bacterial and mammalian systems, both in vivo (animal experiments) and in vitro (test tube experiments). Several of these assays have been complicated by the presence of stabilizers that are known to cause positive responses. Overall, these studies indicate that pure trichloroethylene either has no mutagenic activity or only weak activity under certain conditions. Binding of trichloroethylene, or its metabolites, to protein, RNA, and DNA has been shown in vitro. Extremely low or no binding to DNA

has been reported in vivo. Hence, trichloroethylene does not show significant evidence of genotoxicity in these test systems.

Carcinogenicity

The carcinogenic potential of trichloroethylene in laboratory animals and in humans (through epidemiology studies) has been well studied. It has been shown to cause an increased incidence of liver and lung tumors in certain laboratory mice, and small increases in kidney tumors in male rats in some studies. Because of species differences in metabolism of trichloroethylene, the relevance of these results to humans is uncertain.

Laboratory Animal Studies

There have been a number of studies of the carcinogenic potential of trichloroethylene in mice, rats, and hamsters, providing both positive and negative results. Interpretation of these conflicting results requires careful examination of a number of factors, including variations in the purity of the test substances and difficulties in establishing the maximum tolerated dose.

Gavage (feeding-tube) studies by the National Cancer Institute (NCI) and the National Toxicology Program (NTP) showed an increased incidence of liver tumors in B₆C₃F₁ mice. The doses in these two studies ranged up to 2,339 milligrams per kilogram (mg/kg) per day and 1,000 mg/kg/day, respectively. A gavage study by Henschler in Swiss mice (2,400 mg/kg/day to males, 1,800 mg/kg/day to females), on the other hand, showed no significant increase in tumors, and led the researchers to conclude that the study did not support the conclusion that pure trichloroethylene is carcinogenic under realistic exposure conditions.

A gavage study by NCI in Osborne-Mendel rats (1,097 mg/kg/day) showed no significant increase in tumors. Additional gavage studies in Fischer 344 rats and four other rat strains were judged inadequate by NTP to evaluate the presence or absence of a carcinogenic response.

An inhalation study by Henschler in NMRI mice exposed to up to 500 parts per million (ppm) of trichloroethylene showed no increase in tumors in males. An increase in lymphoma incidence was observed in females, but the authors did not attribute the effect to trichloroethylene exposure. An inhalation study by Fukuda in female ICR mice (up to 450 ppm) showed an increase in lung cancer at higher doses, but the incidence of total lung tumors (benign and malignant) was not significantly increased.

Inhalation studies by Henschler in Wistar rats and Syrian hamsters (up to 500 ppm) showed no increased incidence of

cancer. Additional inhalation studies by Fukuda in female Sprague-Dawley rats (up to 450 ppm) also showed no increase in cancer incidence.

Finally, several studies of trichloroethylene exposure have been conducted by Maltoni in Swiss mice, B₆C₃F₁ mice, and Sprague-Dawley rats. These studies showed a variety of responses, including an increased trend, or incidence, of kidney and Leydig cell tumors in male rats and lung tumors in mice. The Science Advisory Board of the U.S. Environmental Protection Agency (EPA) has indicated, however, that the Maltoni studies are of questionable value because of inadequacies in methodology and in the collection and reporting of the data.

Significance of the Animal Data

Extensive research into the induction of mouse liver tumors has shown that the presence of one or more metabolites of trichloroethylene increases the number of certain intracellular organelles (peroxisomes) in the mouse liver with an associated increase in cell division. Such a cancer mechanism may be “promotional” in nature—that is, trichloroethylene would not contribute to induction of tumors unless they had been initiated by other processes unrelated to exposure to the solvent.

In rats, the liver does not show peroxisome proliferation or other evidence of promotional activity following trichloroethylene exposure. This observation is consistent with the absence of liver tumor induction in long-term toxicity tests in rats. Human liver cells, similarly, do not show increases in peroxisomes in response to treatment with trichloroethylene or its metabolites. Consequently, it appears that the mechanism leading to an increase in mouse liver tumors is unlikely to occur in humans.

Laboratory research indicates that the probable mechanism underlying the increase in mouse lung tumors observed in some inhalation studies also may not be relevant to humans. A specific cell type, the Clara cell, in the mouse lung shows a dramatic cytotoxic response to the substance chloral which is formed in these cells by the metabolism of trichloroethylene by the cytochrome P450 pathway. The formation of mouse lung tumors is believed to result from the repeated cycle of damage and repair in the Clara cell which occurs during the dosing regimen of the cancer study. Human lungs, in contrast, have far fewer Clara cells and exhibit little or no P450 activity. Thus, chloral is not expected to accumulate in human Clara cells.

A marginal increase in kidney tumor incidence was seen in rats in certain experiments. Hypotheses concerning the response of the rat kidney to trichloroethylene administration are being explored experimentally. As discussed below, large, well-conducted epidemiology studies of U.S. workers show

no association between trichloroethylene and kidney cancer.

The species-, sex-, and strain-specific patterns of tumor induction have led to investigations of trichloroethylene metabolism and mechanisms of action. The availability of this new information has prompted the U.S. Environmental Protection Agency (EPA) to initiate a reassessment of the carcinogenic risk associated with exposure to trichloroethylene.

Epidemiology Studies

Studies of U.S. workers exposed to trichloroethylene have consistently indicated no overall increase in cancer risk. A retrospective study of over 7,000 U.S. aircraft maintenance workers followed for an average 25 years failed to demonstrate any significant association between exposure to trichloroethylene and an excess rate of cancer. Two similar studies of 4,700 and 2,300 exposed workers, respectively, found no significant increase in cancer mortality despite additional potential exposure through contaminated groundwater in one of the studies. These and other epidemiology studies on trichloroethylene provide support for the conclusion that trichloroethylene does not pose a risk of cancer, including kidney cancer, under normal conditions of occupational exposure and when products are used in accordance with manufacturers’ instructions.

A recent study of a small number of employees in a German cardboard factory reported a substantial increase in the risk of kidney cancer which appeared to be associated with trichloroethylene exposure. Reviewers of this study have criticized its conclusions because the existence of a cluster of cases was recognizable before the study began. As a result, they note that the study cannot be used as an independent test of an association. A small, case-control study by the same group also appeared to support a link between trichloroethylene exposure and kidney cancer. However, the design of this study also has been heavily criticized, particularly with respect to the selection of control subjects. The results of these studies are not consistent with other larger, well conducted epidemiology studies, none of which has associated trichloroethylene exposure with an increased risk of kidney cancer.

Impairment of the function of the von Hippel-Lindau (VHL) tumor suppressor gene is known to be involved in most cases of human kidney cell cancer. Recently, a German group of researchers has reported a possible association between trichloroethylene exposure and multiple mutations of the VHL gene among kidney cancer patients, including a high proportion of subjects showing a specific “hot spot” mutation. Induction of multiple mutations in a single gene, however, is believed by experts to be highly unlikely to lead to development of a tumor. While experts in the VHL research field believe that a specific “hot spot” mutation could be highly significant, further testing has failed to confirm the original observation.

Cancer Classification

The International Agency for Research on Cancer (IARC) currently classifies trichloroethylene in Group 2A, as a substance considered “probably carcinogenic” to humans. IARC, following its own restrictive classification scheme, concluded that the combination of the results from some of the epidemiology studies provided “limited” evidence of carcinogenicity in humans. The American Conference of Governmental Industrial Hygienists (ACGIH) has classified trichloroethylene in Group A5 (Not Suspected as a Human Carcinogen), however, “since the substance has been demonstrated by well controlled epidemiological studies not to be associated with any increased risk of cancer in exposed humans.”

The National Toxicology Program (NTP) classified trichloroethylene as “reasonably anticipated to be a human carcinogen” in the Ninth Report on Carcinogens. NTP proposed to classify it as a “known human carcinogen” in the Tenth Report on Carcinogens. In December 2000, however, a subcommittee of NTP’s Board of Scientific Counselors rejected this proposal and voted 9-to-1 to retain the classification of “reasonably anticipated.”

EPA’s Science Advisory Board has stated that the weight of the evidence for trichloroethylene does not support classification as a probable human carcinogen (Category B2) under the Agency’s 1986 guidelines for carcinogen risk assessment, and that the uncertainties and moderate nature of the responses should be emphasized. The solvent currently is being reassessed under revised guidelines proposed in April 1996. The revised guidelines provide for greater use of mechanistic data to account for differences in response between test animals and humans observed after exposure to substances like trichloroethylene.

Reproductive and Developmental Toxicity

There have been a number of inconclusive reports of developmental toxicity in populations exposed to trichloroethylene and other chemicals in their drinking water. In an attempt to understand more fully the developmental toxicity of trichloroethylene, HSIA recently sponsored a study designed in conjunction with the federal Agency for Toxic Substances and Disease Registry following EPA guidelines. Pregnant rats were exposed to up to 600 ppm trichloroethylene for 6 hours per day, 7 days per week during gestation. The top dose of 600 ppm was chosen because it is known to result in some toxicity in pregnant rats. No maternal toxicity was observed in the lower doses (50 and 150 ppm) and no evidence of developmental toxicity was observed in the fetuses at any dose.

Several earlier studies evaluated the ability of trichloroethylene to affect the reproductive or developmental process in animals. Inhalation studies in rats, mice, and rabbits at concentrations ranging from 300 ppm to 1,800 ppm showed no significant developmental effects. At 300 ppm, no significant maternal toxicity, embryotoxicity, or fetotoxicity was seen in Sprague-Dawley rats or Swiss-Webster mice. No significant effects were observed in Sprague-Dawley rats exposed to 500 ppm. A nonsignificant increased incidence of hydrocephalus (brain swelling) was seen in New Zealand rabbits exposed to 500 ppm. This effect is now recognized as an artifact of the techniques employed, however, and unrelated to solvent exposure. Slight fetotoxicity and growth depression were seen in Long-Evans rat offspring at 1,800 ppm. A dominant lethal study in mice suggests the absence of any adverse effect on the male reproductive system.

This spectrum of negative animal data indicates that trichloroethylene is unlikely to have an adverse effect on human reproduction or development when handled in accordance with manufacturers’ instructions.

Regulation

A number of federal and state requirements control the use and disposal of trichloroethylene. Some of these requirements are summarized below.

Air

The Clean Air Act Amendments of 1990 significantly revised the provisions of Section 112 relating to the regulation of emissions of hazardous air pollutants. Under the new law, EPA is required to develop national emission standards based on maximum achievable control technology, or MACT, for sources of trichloroethylene and 188 other substances within 10 years. The revised Section 112 also requires EPA to review the need for additional control of regulated sources within 8 years of the implementation of the MACT standard. Trichloroethylene also is regulated as an air toxic in most states.

A standard for halogenated solvent cleaning (degreasing) with trichloroethylene and the other chlorinated solvents was promulgated in December 1994 and became effective for existing sources in December 1997. As a result, all degreasing sources using trichloroethylene will be required to obtain an operating permit from the state regulatory agency. Permitting for small degreasing sources may be deferred until 2004.

EPA has determined that trichloroethylene is an acceptable alternative in many applications for methyl chloroform and

chlorofluorocarbon (CFC) 113, solvents whose production has been phased out because of their potential to deplete stratospheric ozone.

Trichloroethylene is controlled as a volatile organic compound (VOC) under state regulations implementing the national ambient air quality standard for ozone (smog). The available information suggests, however, that trichloroethylene exhibits relatively low photochemical reactivity when compared to many other hydrocarbon solvents.

Water

EPA has established national drinking water regulations setting a maximum contaminant level of 5 micrograms per liter (ug/l), equal to 5 parts per billion (ppb), for trichloroethylene. The maximum contaminant level goal (MCLG) for trichloroethylene is zero. EPA has indicated that “[t]he establishment of an MCLG at zero does not imply that actual harm necessarily occurs to humans at a level somewhat above zero, but rather that zero is an aspirational goal, which includes a margin of safety, within the context of the Safe Drinking Water Act.” Various states also may have drinking water regulations that apply to trichloroethylene.

For various industry categories, EPA has established effluent limitation guidelines, which may contain effluent limitations for trichloroethylene. EPA also has published ambient water quality criteria for trichloroethylene for use by states in developing water quality standards.

Waste

Trichloroethylene waste is considered hazardous under the federal Resource Conservation and Recovery Act (RCRA) and many state laws. The waste must be stored, transported, and disposed of in accordance with applicable RCRA and state requirements.

The reportable quantity (RQ) for releases of trichloroethylene under the Comprehensive Environmental Response, Compensation, and Liability Act (Superfund) is 100 pounds. It is one of several hundred chemicals subject to material safety data sheet (MSDS), inventory, and release reporting under the Emergency Planning and Community Right-to-Know Act

(Title III of the 1986 Superfund Amendments and Reauthorization Act, or SARA).

Occupational Exposure

In 1989, the U.S. Occupational Safety and Health Administration (OSHA) lowered the permissible exposure limit (PEL) for trichloroethylene from 100 ppm to 50 ppm for an 8-hour time-weighted-average (TWA). OSHA also established a short-term (15-minute) exposure limit, or STEL, of 200 ppm. These actions were overturned by a federal court in 1993, and the PELs reverted to the former limits of 100 ppm (8-hour TWA), 200 ppm (ceiling), and 300 ppm (peak). Several states that adopted the lower 1989 limits, however, have not adopted the higher limit.

ACGIH currently recommends threshold limit values (TLVs) of 50 ppm for an 8-hour TWA and 100 ppm for a 15-minute STEL.

Trichloroethylene is subject to the OSHA Hazard Communication Standard, which imposes labeling, material safety data sheet (MSDS), and other requirements on employers and their suppliers.

Beyond Compliance

HSIA does not recommend the use of trichloroethylene in any application, including cold cleaning, unless all applicable workplace, disposal, and other environmental regulatory requirements are met. In addition to complying with these various regulatory requirements, many prudent operators of degreasing and other equipment have elected to adopt practices and standards for the use, management, and disposal of trichloroethylene and trichloroethylene-containing wastes that go beyond the strict legal requirements. These operators recognize that environmental protection is their responsibility. They also understand that they are potentially liable for environmental contamination that can be traced to their solvent wastes, whether at their own plant or elsewhere, regardless of the fact that they may have complied with the letter of the law. These operators recognize that additional measures that go “Beyond Compliance” make good business sense because they minimize the risks of liability that arise when trichloroethylene is released to the environment.

Regulatory and Technical Information for Trichloroethylene

Chemical Formula	C ₂ HCl ₃
Molecular Weight	131.4
CAS Number	79-01-6
Boiling Point	189°F (87°C)
Weight per Gallon @77°F	12.11
Flash Point	none
Flammability Limits @ 77°F (% solvent in air, by volume)	
Lower Limit	8.0
Upper Limit	9.2 (vapor saturation point)
Flammability Limits @ 212°F (% solvent in air, by volume)	
Lower Limit	8.0
Upper Limit	44.8
Solubility @ 77°F (grams/100 grams)	
Trichloroethylene in water	0.10
Water in trichloroethylene	0.04
OSHA PEL (see discussion in text)	
8-hour TWA	100 ppm
Ceiling	200 ppm
Peak	300 ppm
ACGIH TLV	
8-hour TWA	50 ppm
15-minute STEL	100 ppm
Cancer Classification	
ACGIH	A5
IARC	2A
NTP	"reasonably anticipated"
CERCLA Reportable Quantity	100 lbs
Maximum Contaminant Level	5 ppb (5 ug/l)
RCRA Hazardous Waste No.	U 228
Department of Transportation	
Hazard Class	6.1 (packing group III)
ID Number	UN 1710
